Search Results -

Term	Documents
ANTISENSE.USPT.	8456
ANTISENSES.USPT.	8
(1 AND ANTISENSE).USPT.	219

Database: US Patents Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: `l1 and antisense` Clear

Search History

Today's Date: 10/16/2000

DB Name	Query	Hit Count	Set Name
USPT	l1 and antisense	219	L2
USPT	hyaluronic	2887	L1

Search Results -

Term	Documents
VEGF.USPT.	481
VEGFS.USPT.	4
(2 AND VEGF).USPT.	20

Database: US Patents Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: `l2 and vegf` Clear

Search History

Today's Date: 10/16/2000

DB Name	Query	Hit Count	Set Name
USPT	l2 and vegf	20	L3
USPT	l1 and antisense	219	L2
USPT	hyaluronic	2887	L1

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FILE LAST UPDATED: OCT 2000 (20001012/UP). FILE [redacted]VERS 1960 TO DATE.

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=> s hyaluronic

L1 8272 HYALURONIC

=> s l1 and antisense

12360 ANTISENSE
L2 8 L1 AND ANTISENSE

=> d 1-8 ab

L2 ANSWER 1 OF 8 MEDLINE
AB Malignant mesothelioma characteristically shows epithelial and/or sarcomatous morphology, this phenotypic differentiation being correlated to the prognosis. The present study was undertaken to see whether proteoglycan (PG) expression influences mesothelioma differentiation. To assess this hypothesis, we studied a mesothelioma model, where the cells were induced to differentiate into epithelial or fibroblast-like morphology, mimicking the biphasic growth of this sarcoma. Series of PGs were analyzed in parallel by semiquantitative reversed transcriptase polymerase chain reaction, showing increased expression of syndecan-2, syndecan-4, and hyaluronan synthase in the epithelial phenotype, whereas the fibroblast-like cells expressed more matrix PGs: versican, decorin, and biglycan. Western blotting confirms these differences and provides evidence of extensive shedding and rapid turnover of cell membrane PGs. Experimental down-regulation of the studied syndecans by **antisense** targeting resulted in a change in shape from polygonal to spindle-like morphology, while syndecan-1 and -4, but not syndecan-2, could be associated with cell aggregation, indicating distinct functions of different syndecans. The PG profile is thus closely associated with the morphology and biological behavior of tumor cells, mesotheliomas showing a different profile than true epithelial tumors.

L2 ANSWER 2 OF 8 MEDLINE
AB CD44 is a cell surface glycoprotein involved in cell migration and cell docking in target organs via interactions with various ligands, including **hyaluronic** acid (HA), which is the principal ligand of this receptor. Alternative splicing generates many isoforms of CD44, including standard CD44 (CD44s) and CD44 variants (CD44v). LB T-cell lymphoma, which predominantly expresses CD44s, acquires additional CD44v and HA binding capacity after activation with phorbol ester. The HA9 cell line, isolated from parental LB cells, expresses CD44v and constitutively binds HA. Downregulation of CD44v isoforms of HA9 cells, by CD44v specific **antisense** inhibited their ability to bind HA, indicating that CD44v, rather than CD44s, is associated with the activation status of this molecule. Using the reverse transcriptase polymerase chain reaction, we

found that LB cells after infiltrating spleen and lymph nodes of BALB/c mice, contain [redacted]enriched repertoire of CD44v, [redacted]lying that the metastatic cell[redacted] acquired the activated form of this receptor.

L2 ANSWER 3 OF 8 MEDLINE
AB The lesions of fibrocontractive diseases result from an excessive myofibroproliferative response to numerous forms of inflammatory stimuli, which elicit the net deposition of extracellular matrix (ECM) in the interstitium of the affected tissue. Hyaluronan (HA), reported to be a key player supporting cellular migration and adherence, is a major component of ECM that undergoes dynamic regulation during inflammation. The molecular regulation of HA biosynthesis by inflammatory cytokines on myofibroblasts is not yet completely understood. Here we report the biochemical characteristics of the lung myofibroblast cell line MRC-5, and we demonstrate that the production of HA by this cell line is inducible by the proinflammatory cytokine, tumor necrosis factor-alpha (TNF-alpha), at the message level of HA synthase (HAS). In TNF-alpha-stimulated MRC-5 cells, DNA-binding and competition experiments indicated that the predominant NF-kappa B binding activity detected with nuclear extract-stimulated cells is mediated by the p50/p65 complex. Using **antisense** oligonucleotides, we confirmed that the TNF-alpha-stimulation of HA synthesis by MRC-5 cells is dependent on the activation of the p50/p65 NF-kappa B complex. These findings indicate that TNF-alpha production within inflamed tissues may enhance the HA synthesis via the transcriptional induction of HAS on myofibroblasts, thereby providing a provisional matrix for supporting cellular migration and adhesion, and that the p50/p65 NF-kappa B complex that plays an important role in the regulation of HA production by TNF-alpha might be an appropriate target for therapeutic compounds to treat tissue fibrosis accompanied by inflammation.

L2 ANSWER 4 OF 8 MEDLINE
AB CD44 is a broadly distributed polymorphic glycoprotein that serves as the principal cell-surface receptor for hyaluronate. Although CD44-mediated cell interaction with hyaluronate has been implicated in a variety of physiologic events, including cell-cell and cell-substrate adhesion, cell migration, proliferation, and activation, as well as hyaluronate uptake and degradation, the biologic role of CD44 in vivo in various tissues remains to be determined. In the present work we have developed transgenic mice that express an **antisense** CD44 cDNA driven by the keratin-5 promoter. These mice lack detectable CD44 expression in skin keratinocytes and corneal epithelium and display abnormal hyaluronate accumulation in the superficial dermis and corneal stroma, distinct morphologic alterations of basal keratinocytes and cornea, and defective keratinocyte proliferation in response to mitogen and growth factors. These alterations are reflected by a decrease in skin elasticity, impaired local inflammatory response and tissue repair, delayed hair regrowth, and failure of the epidermis to undergo hyperplasia in response to carcinogen. Our observations indicate that two major functions of CD44 in skin are the regulation of keratinocyte proliferation in response to extracellular stimuli and the maintenance of local hyaluronate homeostasis.

L2 ANSWER 5 OF 8 MEDLINE
AB We demonstrate in this report that the Xenopus DG42 gene product made in the yeast Saccharomyces cerevisiae can synthesize authentic high molecular

weight hyaluronan (**hyaluronic** acid; HA) in vitro. Saccharomyces are eukaryotes that do not naturally produce HA or any other molecules known to contain glucuronic acid. Therefore bakers' yeast is a good model system to determine the enzymatic activity of the DG42 protein, which is the topic of recent debate. Membrane extracts prepared from cells expressing DG42 encoded on a plasmid incorporated [14C]glucuronic acid and N-[3H]acetylglucosamine from exogenously supplied UDP-sugar nucleotides into a high molecular mass (10(6) to 10(7) Da) polymer in the presence of magnesium ions. Both sugar precursors were simultaneously required for elongation. Control extracts prepared from cells with the vector plasmid alone or the DG42 cDNA in the **antisense** orientation did not display this activity. The double-labeled polysaccharide product synthesized in vitro was deemed to be HA by enzymatic analyses; specific HA lyase could degrade the polymer, but it was unaffected by protease or chitinase treatments. The fragments generated by HA lyase were identical to fragments derived from authentic vertebrate HA as compared by high performance liquid chromatography. We conclude that DG42 is a membrane-associated HA synthase capable of transferring both glucuronic acid and N-acetylglucosamine groups.

L2 ANSWER 6 OF 8 MEDLINE

AB The hyaluronan (HA) receptor RHAMM is an important regulator of cell growth. Overexpression of RHAMM is transforming and is required for H-ras transformation. The molecular mechanism underlying growth control by RHAMM and other extracellular matrix receptors remains largely unknown. We report that soluble RHAMM induces G2/M arrest by suppressing the expression of Cdc2/Cyclin B1, a protein kinase complex essential for mitosis. Down-regulation of RHAMM by use of dominant negative mutants or **antisense** of mRNA also decreases Cdc2 protein levels. Suppression of Cdc2 occurs as a result of an increased rate of cdc2 mRNA degradation. Moreover, tumor cells treated with soluble RHAMM are unable to form lung metastases. Thus, we show that mitosis is directly linked to RHAMM through control of Cdc2 and Cyclin B1 expression. Failure to sustain levels of Cdc2 and Cyclin B1 proteins leads to cell cycle arrest.

L2 ANSWER 7 OF 8 MEDLINE

AB TGF-beta is a potent stimulator of motility in a variety of cell types. It has recently been shown that hyaluronan (HA) can directly promote locomotion of cells through interaction with the HA receptor RHAMM. We have investigated the role of RHAMM and HA in TGF-beta-stimulated locomotion and show that TGF-beta triggers the transcription, synthesis and membrane expression of the RHAMM receptor and the secretion of HA coincident with the induction of the locomotory response. This was demonstrated by both incubating cells with exogenous TGF-beta 1 and by stimulating the production of bioactive TGF-beta 1 in tumor cells transfected with TGF-beta 1 under the control of the metallothionein promoter. TGF-beta 1-induced locomotion was suppressed by antibodies that prevented HA/RHAMM interaction, using polyclonal antibodies to either RHAMM fusion protein or RHAMM peptides, or mAbs to purified RHAMM. Peptides corresponding to the HA-binding motif of RHAMM also suppressed TGF-beta 1-induced increases in motility rate. Spontaneous locomotion of fibrosarcoma cells was blocked by neutralizing secreted TGF-beta with panspecific TGF-beta antibodies and by inhibition of TGF-beta 1 secretion with **antisense** oligonucleotides. Polyclonal anti-RHAMM fusion protein antibodies and peptide from the RHAMM HA-binding motif also suppressed the spontaneous motility rate of fibrosarcoma cells. These data suggest that fibrosarcoma cell locomotion requires TGF-beta, and the pathway by which TGF-beta stimulates locomotion uses the HA receptor RHAMM and HA.

L2 ANSWER 8 OF 8 MEDLINE
AB We have obtained the complete coding sequence of neurocan, a chondroitin sulfate proteoglycan of rat brain which is developmentally regulated with respect to its molecular size, concentration, carbohydrate composition, sulfation, and immunocytochemical localization. Two degenerate oligonucleotides, based on amino acid sequence data from the proteoglycan isolated from adult brain by immunoaffinity chromatography with the 1D1 monoclonal antibody, were used as sense and **antisense** primers in the polymerase chain reaction with a brain cDNA library as template to generate an unambiguous cDNA probe. A second probe for the N-terminal portion of the early postnatal form of the proteoglycan was obtained by reverse transcription/polymerase chain reaction. The composite sequence of overlapping cDNA clones is 5.2-kilobases (kb) long, including 1.3 kb of 3'-untranslated sequence and 76 base pairs of 5'-untranslated sequence. An open reading frame of 1257 amino acids encodes a protein with a molecular mass of 136 kDa containing 10 peptide sequences present in the adult and/or early postnatal brain proteoglycans. The deduced amino acid sequence revealed a 22-amino acid signal peptide followed by an immunoglobulin domain, tandem repeats characteristic of the **hyaluronic** acid-binding region of aggregating proteoglycans, and an RGDS sequence. The C-terminal portion (amino acids 951-1215) has approximately 60% identity to regions in the C termini of the fibroblast and cartilage proteoglycans, versican and aggrecan, including two epidermal growth factor-like domains, a lectin-like domain, and a complement regulatory protein-like sequence. The central 595-amino acid portion of neurocan has no homology with other reported protein sequences.
The proteoglycan contains six potential N-glycosylation sites and 25 potential threonine O-glycosylation sites. In the adult form of the proteoglycan (which represents the C-terminal half of neurocan) a single 32-kDa chondroitin 4-sulfate chain is linked at serin-944, whereas three additional potential chondroitin sulfate attachment sites (only two of which are utilized) are present in the larger proteoglycan species. A probe corresponding to a region of neurocan having no homology with versican or aggrecan hybridized with a single band at approximately 7.5 kb on Northern blots of mRNA from both 4-day and adult rat brain (but not with muscle, kidney, liver, or lung mRNA), indicating that the 1D1 proteoglycan of adult brain, containing a 68-kDa core protein, is generated by a developmentally regulated in vivo proteolytic processing of the 136-kDa species which is predominant in early postnatal brain.(ABSTRACT TRUNCATED AT 400 WORDS)

=> d 1-8

L2 ANSWER 1 OF 8 MEDLINE
AN 2000386509 MEDLINE
DN 20367911
TI Differentiation of mesothelioma cells is influenced by the expression of proteoglycans.
AU Dobra K; Andang M; Syrokou A; Karamanos N K; Hjerpe A
CS Department of IMPI, Karolinska Institutet, Huddinge University Hospital, Stockholm, Sweden.
SO EXPERIMENTAL CELL RESEARCH, (2000 Jul 10) 258 (1) 12-22.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals

EM 200010
EW 20001002

L2 ANSWER 2 OF 8 MEDLINE
AN 2000218047 MEDLINE
DN 20218047
TI The CD44 receptor of the mouse LB T-cell lymphoma: analysis of the isoform
repertoire and ligand binding properties by reverse-transcriptase polymerase chain reaction and **antisense** oligonucleotides.
AU Wallach S B; Friedmann A; Naor D
CS The Lautenberg Center for General and Tumor Immunology, Hebrew University-Hadassah Medical School, Jerusalem, Israel.
SO CANCER DETECTION AND PREVENTION, (2000) 24 (1) 33-45.
Journal code: CNZ. ISSN: 0361-090X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
EW 20000803

L2 ANSWER 3 OF 8 MEDLINE
AN 1999144105 MEDLINE
DN 99144105
TI Stimulation of hyaluronan synthesis by tumor necrosis factor-alpha is mediated by the p50/p65 NF-kappa B complex in MRC-5 myofibroblasts.
AU Ohkawa T; Ueki N; Taguchi T; Shindo Y; Adachi M; Amuro Y; Hada T; Higashino K
CS Third Department of Internal Medicine, Hyogo College of Medicine, Japan.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1999 Jan 11) 1448 (3) 416-24.
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199905
EW 19990501

L2 ANSWER 4 OF 8 MEDLINE
AN 97282619 MEDLINE
DN 97282619
TI Selective suppression of CD44 in keratinocytes of mice bearing an **antisense** CD44 transgene driven by a tissue-specific promoter disrupts hyaluronate metabolism in the skin and impairs keratinocyte proliferation.
AU Kaya G; Rodriguez I; Jorcano J L; Vassalli P; Stamenkovic I
CS Department of Pathology, University Medical Center, University of Geneva, Switzerland.
NC CA55735 (NCI)
SO GENES AND DEVELOPMENT, (1997 Apr 15) 11 (8) 996-1007.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199707

L2 ANSWER 5 OF 8 MEDLINE
AN 96394480 MEDLINE
DN 96394480
TI Yeast-derived recombinant DG42 protein of Xenopus can synthesize hyaluronan in vitro.
AU DeAngelis P L; Achyuthan A M
CS Department of Biochemistry and Molecular Biology, University of Oklahoma

Health Sciences Center, Oklahoma City, Oklahoma 73190, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Sep 27) 271 (39) 23657-60.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-A54926; GENBANK-A46089
EM 199701
EW 19970104

L2 ANSWER 6 OF 8 MEDLINE
AN 96261667 MEDLINE
DN 96261667
TI Soluble hyaluronan receptor RHAMM induces mitotic arrest by suppressing Cdc2 and cyclin B1 expression.
AU Mohapatra S; Yang X; Wright J A; Turley E A; Greenberg A H
CS Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Apr 1) 183 (4) 1663-8.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610

L2 ANSWER 7 OF 8 MEDLINE
AN 94043455 MEDLINE
DN 94043455
TI TGF-beta 1 stimulation of cell locomotion utilizes the hyaluronan receptor
RHAMM and hyaluronan.
AU Samuel S K; Hurta R A; Spearman M A; Wright J A; Turley E A; Greenberg A H
CS Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, Canada.
NC CA51540 (NCI)
SO JOURNAL OF CELL BIOLOGY, (1993 Nov) 123 (3) 749-58.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199402

L2 ANSWER 8 OF 8 MEDLINE
AN 92406907 MEDLINE
DN 92406907
TI Cloning and primary structure of neurocan, a developmentally regulated, aggregating chondroitin sulfate proteoglycan of brain.
AU Rauch U; Karthikeyan L; Maurel P; Margolis R U; Margolis R K
CS Department of Pharmacology, New York University Medical Center, New York 10016..
NC NS-09348 (NINDS)
NS-13876 (NINDS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Sep 25) 267 (27) 19536-47.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-M97161; GENBANK-S76077; GENBANK-S76125; GENBANK-S76126; GENBANK-D11148; GENBANK-D11149; GENBANK-D11150; GENBANK-D11151; GENBANK-D10347; GENBANK-D10348